

# Intraoperative Radiotherapy in Locally-Advanced and Recurrent Rectal Cancer: Retrospective Review of 68 Cases

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## Introduction

The addition of intraoperative radiation therapy (IORT) to the multimodal treatment of locally advanced or recurrent rectal cancer may improve local control. Although electron beam IORT is the most common modality, technological advances now permit the use of photon beam IORT. However, few studies have investigated these devices in rectal cancer. The **PURPOSE** of this study was to analyze the feasibility and effectiveness of IORT in locally advanced or recurrent rectal cancer, and clinical outcome of patients receiving surgery and radiotherapy using our design.

## Methods and Materials

Retrospective review of patients (pts) treated with surgery and IORT for stage T3-T4 rectal cancer or pelvic recurrence between December 2012 and December 2014. Patients with distant metastasis were excluded. IORT was delivered with the Intrabeam Photon Radiosurgery System (PRS). The study sample included 68 patients (41 males, 27 females) ranging in age from 33 to 82 years (median, 67). Most patients (47) had stage II primary rectal cancer (PRC), while 21 pts had stage III disease. Nine of this pts presented recurrent rectal cancer (RRC). Wanebo staging for the 9 PRC cases was: Tr3 (6 pts), Tr4 (2 pts), and Tr5 (1 pt). A dose of 5.07 Gy was prescribed to a depth of 1 cm (surface dose range was 9.4-17.0, median 14.8 Gy). Median duration of IORT was 31.9 minutes (range 15-36). The spherical applicator was 5 cm in diameter in 61 cases and 4.5 in 7 cases. A subgroup analysis (23 pts) was performed to assess those pts with the longest follow up (range, 17 - 28 months; median, 20.7). Of these, 18/23 (78%) received adjuvant chemotherapy. Overall survival (OS) and disease-free survival were calculated with the Kaplan-Meier method.

**Table 1. Disease and Characteristics of Patients**

|  |             |         |
|--|-------------|---------|
| Total number of patients               |             | 68      |
| Gender                                 | M           | 41      |
|  | F           | 27      |
| Age, years                             |             | 33 - 76 |
| Mean age, years                        |             | 59      |
| Primary cancer                         |             | 59      |
| Recurrent Tumor                        |             | 9       |
| Stage (initial tumor)                  | II          | 47      |
|  | III         | 21      |
|  | II          | 3       |
| Tumor staging (for recurrent cases)    | III         | 6       |
|  | TR3         | 6       |
|  | TR4         | 2       |
|  | TR5         | 1       |
| Recurrent tumor state by Wanebo        |             |         |
|  | Adeno CA G1 | 13      |
|  | G2          | 32      |
|  | G3          | 23      |
| External-beam radiotherapy before IORT | Yes         | 11      |
|  | No          | 57      |
| Chemotherapy before IORT               | Yes         | 8       |
|  | No          | 60      |

## Design of the Radiotherapy

| Option                                | Indicants |
|---------------------------------------|-----------|
| Surface dose, Gy                      | 14,6      |
| Depth dose 0,5 cm, Gy                 | 8,1       |
| Depth dose 1,0 cm Gy                  | 5,07      |
| IORT duration min - max, minutes      | 25 - 36   |
| Medium IORT duration, minutes         | 32        |
| Operation duration min - max, minutes | 175 - 270 |
| Medium operation duration, minutes    | 186       |

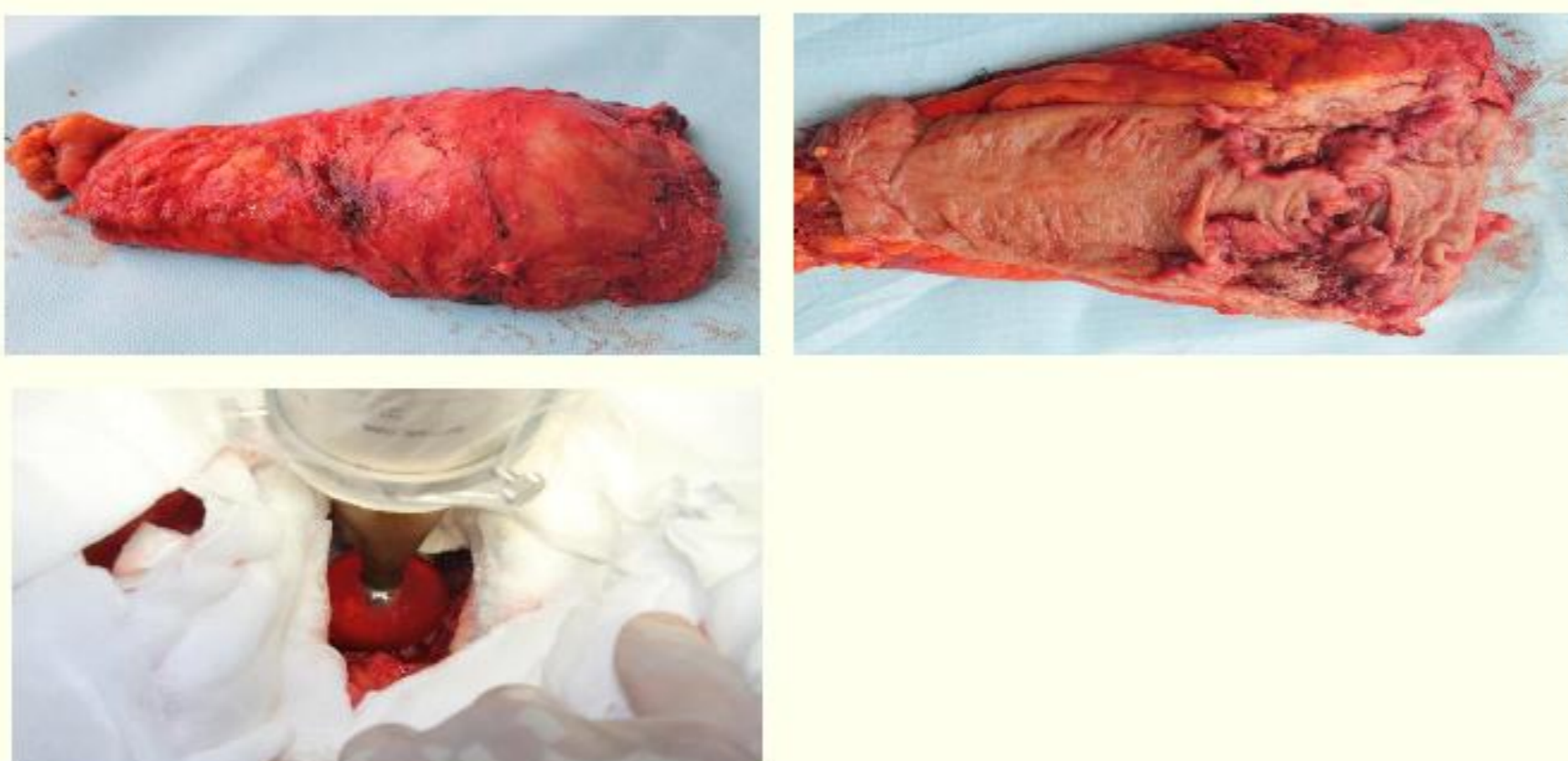
**Figure 1. Intrabeam preparation for IORT**



**Figure 2. Shielding of the Operative Field**



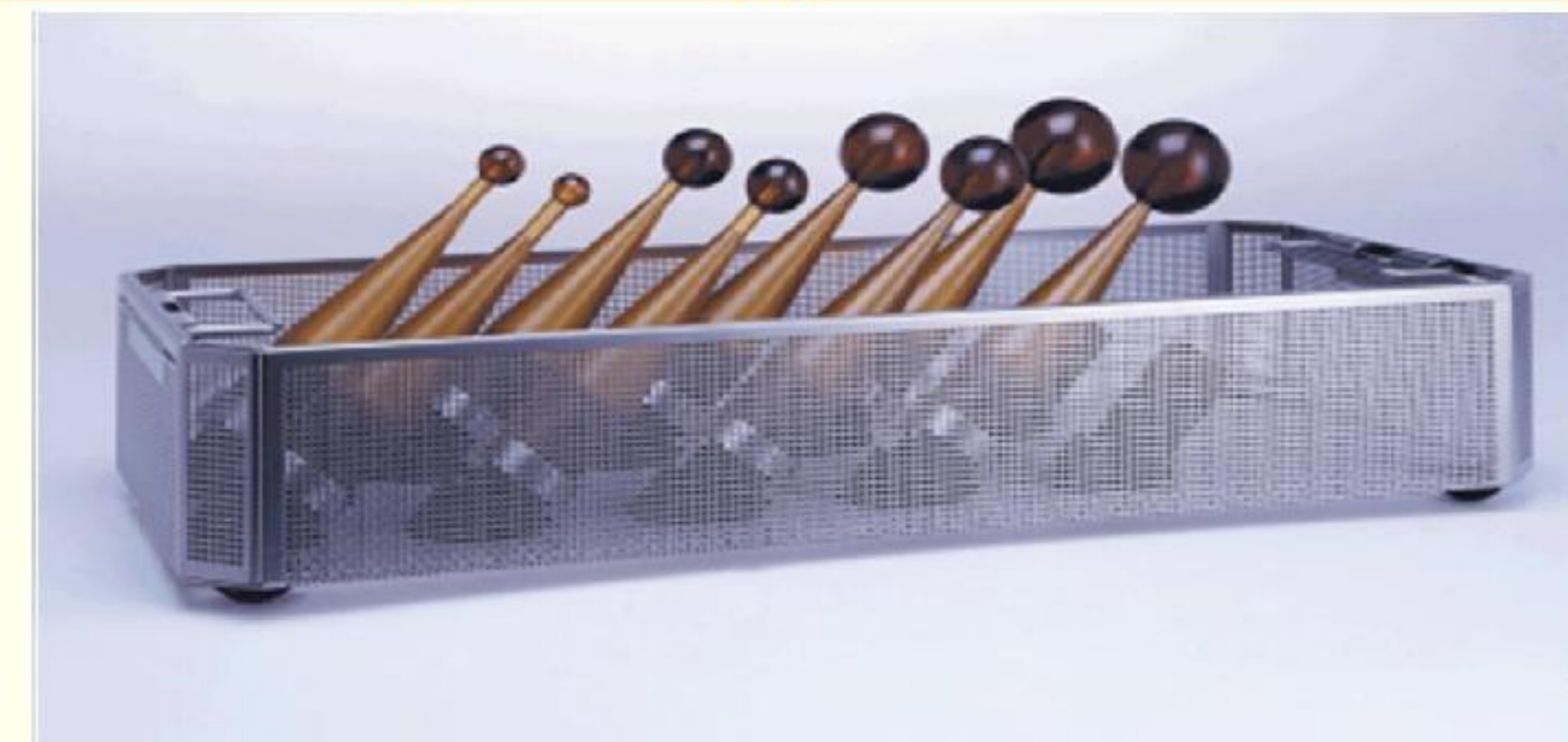
**Figure 3. Specimen after TME and the Applicator installation to the Tumor Bed**



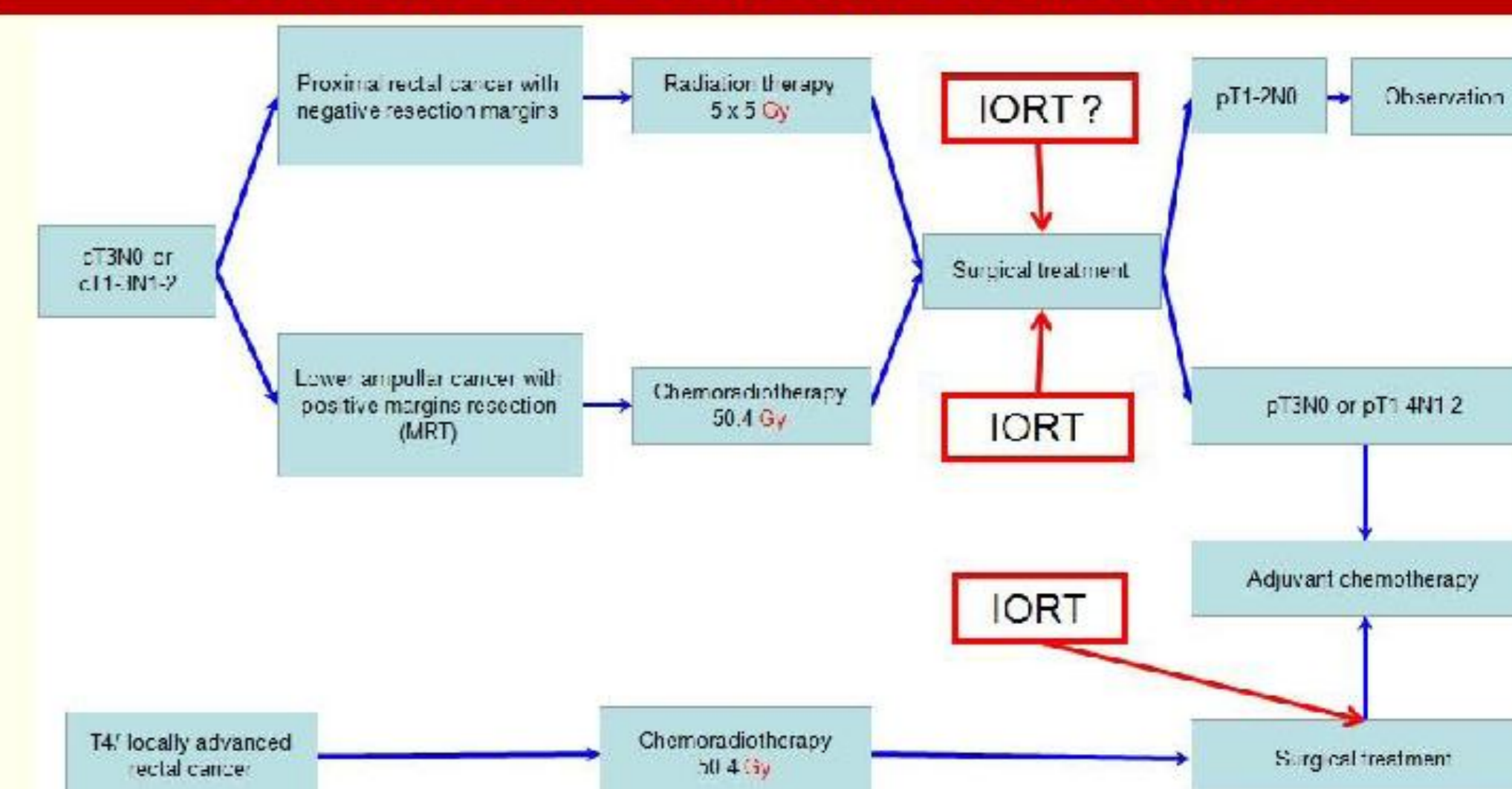
**Table 3. Diameter of Applicators used in 68 Patients**

| Diameter | n  |
|----------|----|
| 4,0 cm   | 2  |
| 4,5 cm   | 7  |
| 5,0 cm   | 59 |

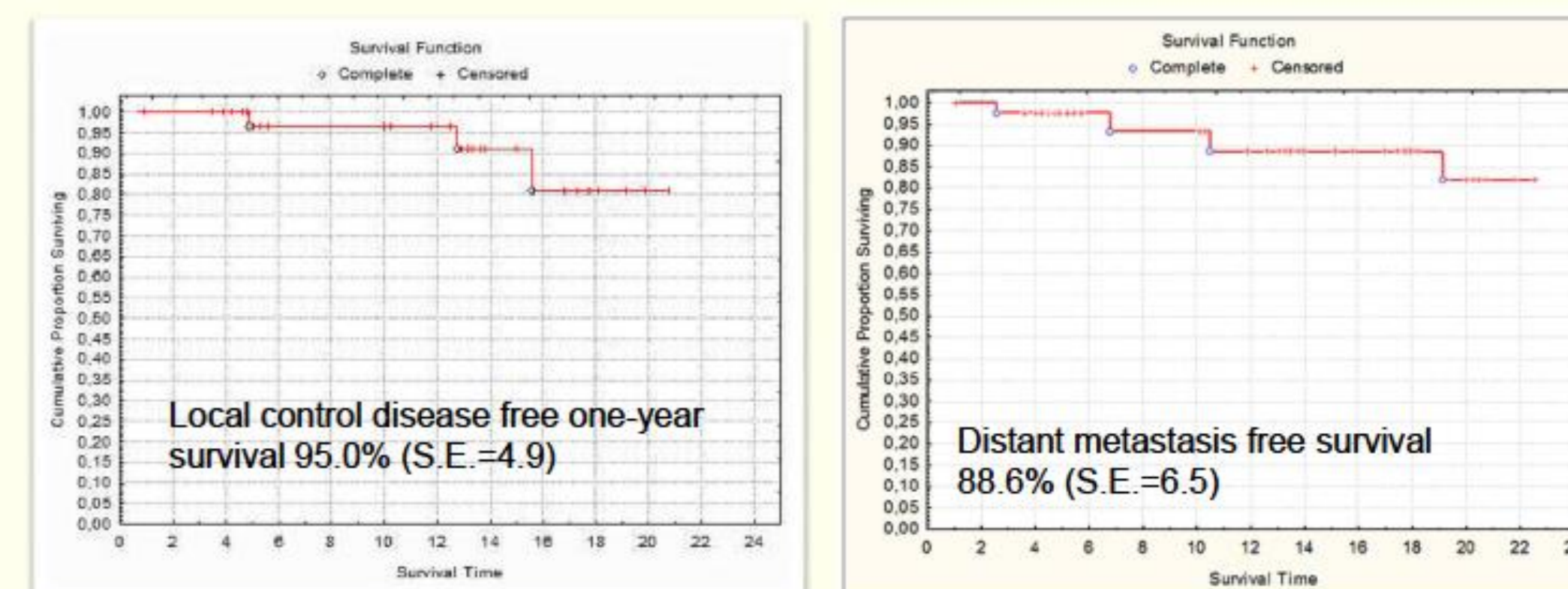
**Figure 4. Applicators Set**



**Figure 5. IORT in the algorithm of the combined rectal cancer treatment**



**Figure 6. Kaplan-Meier Curves of the 2 Years DFS and MFS**



## Results

In 18 of the 68 patients (26.4%), the tumour was attached to the sidewall. Margins were positive in 7 patients (10.3%). In the 23 pt's subgroup with long-term follow up, OS was 87.0%. Local recurrence occurred in 3 of 23 pts (13%). Four cases (17.4%) of distant metastasis (lung: 3 cases; liver: 1 case) were recorded. No intraoperative complications attributable to IORT were registered. Median postsurgical discharge time was 17.7 days (range: 9-25). No cases of hydronephrosis or ureter fibrosis after IORT were documented.

**Table 2. IORT long term follow up 15.2 to 26.2 month (20.3 mean) of 23 patients from Dec. 2012 to Dec. 2013**

| No | Date of surgery | Last sensed | Days | Month follow up | Death      | Recurrence/ Distant MTS | Stage | Age  | Gender |
|----|-----------------|-------------|------|-----------------|------------|-------------------------|-------|------|--------|
| 1  | 18.12.2012      | 23.02.2015  | 785  | 26,2            |            |                         | IIB   | 73   | F      |
| 2  | 26.02.2013      | 16.05.2014  | 440  | 14,7            | 16.05.2014 | MTS lungs               | III A | 63   | M      |
| 3  | 25.06.2013      | 09.04.2015  | 644  | 21,5            |            |                         | IIB   | 75   | F      |
| 4  | 04.07.2013      | 30.03.2015  | 626  | 20,9            |            |                         | IIA   | 48   | F      |
| 5  | 08.07.2013      | 16.07.2014  | 368  | 12,3            | 16.07.2014 |                         | III B | 50   | M      |
| 6  | 01.08.2013      | 12.03.2015  | 581  | 19,4            |            | MTS lungs               | IIA   | 74   | M      |
| 7  | 22.08.2013      | 04.04.2015  | 582  | 19,4            |            |                         | II C  | 67   | M      |
| 8  | 10.07.2013      | 25.01.2015  | 555  | 18,5            |            |                         | IIA   | 67   | F      |
| 9  | 08.10.2013      | 28.02.2015  | 500  | 16,7            |            |                         | IIA   | 72   | M      |
| 10 | 26.06.2013      | 31.01.2015  | 575  | 19,2            |            |                         | IIIB  | 62   | M      |
| 11 | 10.01.2013      | 10.03.2015  | 780  | 26,0            |            |                         | II    | 47   | M      |
| 12 | 11.02.2013      | 11.03.2015  | 750  | 25,0            |            |                         | II    | 70   | M      |
| 13 | 20.02.2013      | 08.02.2015  | 708  | 23,6            |            |                         | III A | 76   | F      |
| 14 | 25.02.2013      | 24.03.2015  | 749  | 25,0            |            |                         | II    | 63   | M      |
| 15 | 05.03.2013      | 14.02.2015  | 699  | 23,3            |            |                         | II    | 76   | F      |
| 16 | 20.03.2013      | 27.01.2015  | 667  | 22,2            |            | MTS lungs               | IV    | 58   | M      |
| 17 | 15.05.2013      | 09.03.2015  | 654  | 21,8            |            |                         | III A | 51   | M      |
| 18 | 24.04.2013      | 27.03.2015  | 693  | 23,1            |            | Local recurrence        | III A | 33   | F      |
| 19 | 19.06.2013      | 26.02.2015  | 607  | 20,2            |            | Local recurrence        | II    | 54   | M      |
| 20 | 17.07.2013      | 22.10.2014  | 455  | 15,2            | 22.10.2014 | Local recurrence        | II    | 75,0 | M      |
| 21 | 30.07.2013      | 14.02.2015  | 554  | 18,5            |            |                         | II    | 74,0 | F      |
| 22 | 09.10.2013      | 23.02.2015  | 494  | 16,5            |            | MTS liver               | II    | 58,0 | M      |
| 23 | 15.10.2013      | 01.04.2015  | 526  | 17,5            |            |                         | III A | 82   | M      |

## Conclusions

The initial results presented here suggest that the Intrabeam Photon Radiosurgery System is a safe technology for use in IORT in the multimodal treatment of rectal cancer. IORT with PRS marginally increased operative time, and did not appear to prolong hospitalization. Our rates of long-term toxicity, local recurrence, and survival rates compare favorably with published reports of IORT delivery with other methods. However, future studies are needed to report long term results of this system in rectal cancer.

## Keywords

Colorectal cancer, intraoperative radiation therapy, local disease recurrence.

## References

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